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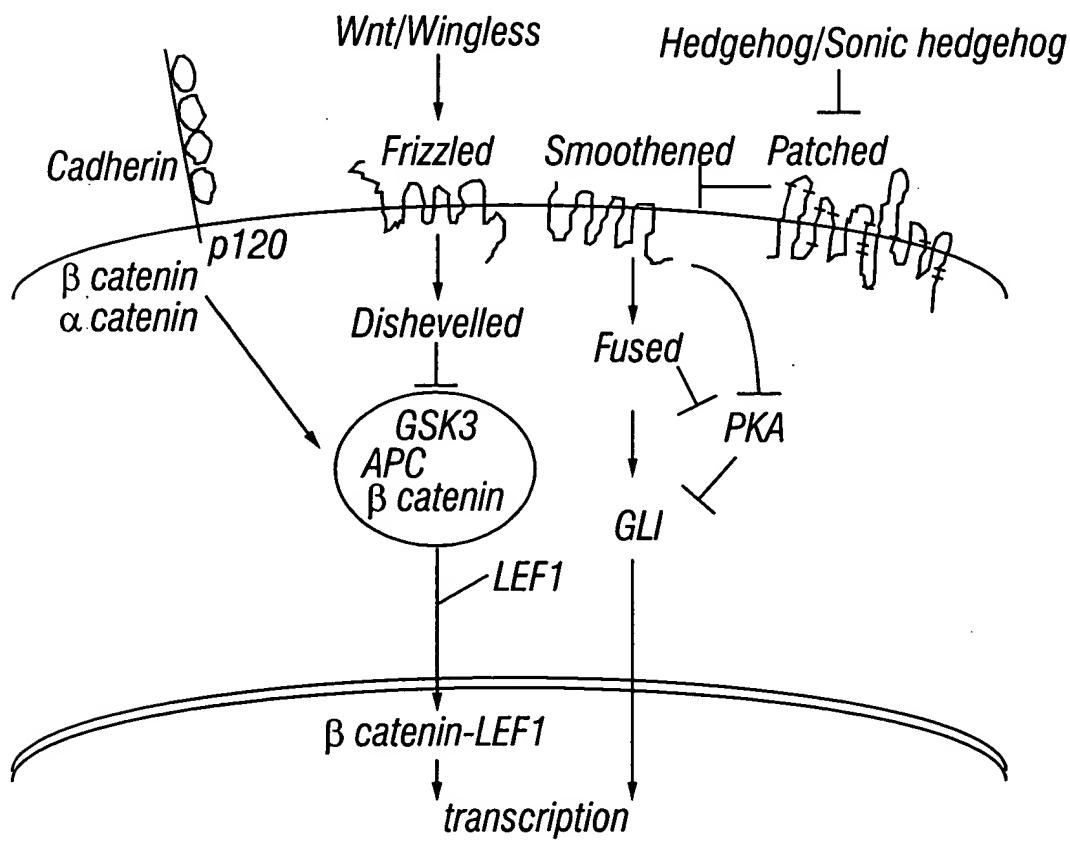


FIG. 1

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Alignment of several frizzled family members

→ amino terminal domain

fz3/mouse	-----MAWSWIVFDLWLLTVFLG--QIGGHS-----LFSCE
fz4/mouse	-----MAWPGTGPS---SRGAPGGVGLRLGLLQFLLLRPTLGFCD-----EEERRCD
fz8/mouse	-----MEWGYL----LEVTSLAALAVLQRSSG-AAAASK-----ELACQ
fz5/human	-----MARPDPA---SAPPSSLL--LLLLAQLVG-RAAAASK-----APVCQ
fzd9/human	-----MAVAPLRLGALLWQLLAAGGAALEIGRFD-----PERGRG-----AAPCQ
fz1/rat	LEAPLLLGVRAQPAG---QVSG-PGQQRPPPPQPPQQGG--QQYNGERG--ISIPDHGQCY
fz2/rat	-----MRARSAL---PRSALPRLLLPLLPAAGP--AQFHGEKG--ISIPDHGFCQ
fz/Dros	ILPTLIQGVQRYDQS---PLDASPYYRSGGGLMASSG---TELDG-----LPHHNRCE
fz2/Dros/	GLVLLLTSCRADGPL----HSADHGMGGMGMGGHGLD-ASPAPGYGVPAIPKDPNLRCE

CRD

fz3/mouse	PITLRMCQDLPYNTTFMPNLLNHYDQTAALAMEPFHPMVNLDCSRDFRPFLCALYAPIC
fz4/mouse	PIRIAMCQNLGYNVTKMPNLVGHELQTDALQLTTFTPLIQQGCSQLQFFLCSVYVPMC
fz8/mouse	EITVPLCKGIGNYTYMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPDLKFFLCSMYTPIC
fz5/human	EITVPMCRGIGYNLTHMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPDLRFFLCTMYTPIC
fzd9/human	AVEIPMCRGIGYNLTRMPNLLGHTSQGEAAAELAEFAPLVQYGHSHLRFFLCSLYAPMC
fz1/rat	PISIPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVC
fz2/rat	PISIPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFPLCSMYAPVC
fz/Dros	PITISICKNIPYNMTIMPNLIGHTKQEEAGLEVHQFAPLVKIGCSDDLQLFLCSLYVPVC
fz2/Dros/	EITIPMCRGIGYNMTSFPNEMNHETQDEAGLEVHQFWPLVEIKCSPDLKFFLCSMYTPIC
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CRD

fz3/mouse	M-EYGRVTLPCRRLCQRAYSECSKLMEMFG-VPWPEDMECSRFPDCD-EPYPRLVLDL--
fz4/mouse	TEKINIPIGPCGGMCLSVKRRCEPVLREFG-FAWPDTLNCSKFPQDN-DHNMCMEGP--
fz8/mouse	LEDYKKPLPPCRSVCERAKAGCPLMRQYG-FAWPDRMRCDRLPEQG-NPDTLCMDYN-R
fz5/human	LPDYHKPLPPCRSVCERAKAGCPLMRQYG-FAWPERMCDRLPVLGRDAEVLCMDYN-R
fzd9/human	TDQVSTPIPACRPMCEQARLRCAPIMEQFN-FGWPDSLDCARLPTRN-DPHALCMEA PEN
fz1/rat	T-VLEQALPPCRSLCERA-QGCEALMNKFG-FQWPDTLKCEKFPVHG--AGELCVGQNTS
fz2/rat	T-VLEQAIPPCRSICERARQGCEALMNKFG-FQWPERLRCEHFPRHG--AEQICVGQNH S
fz/Dros	T-ILERPIPPCRSLCESA-RVCEKLMKTYN-FNWPNLECSKFPVHG--GEDLCVAENTT
fz2/Dros/	LEDYHKPLPVCRSVCERARSGCPLMOOYS-FEWPERMACEHPLHG-DPDNLCLMEOPSY

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FIG. 2A

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fz3/mouse	-----LVGDPTE-----
fz4/mouse	---GDEE-----VPLPHKTP-
fz8/mouse	TDLTTAAPSPRRLPPPPPGEQPPSGSGHSRPPGARPPHRGGSSRGSGDAAAAPPSRGG
fz5/human	SEATTAPPRP---FPAKP---TLP---G---PP-----G---APAS-GG
fzd9/human	ATAGPAEPHK---GLGM---LP-----VAPRPARPPG
fz1/rat	DKGTPTPSL-----L-----PEFWTSNPQHG
fz2/rat	EDG---TPAL-----L-----TTAPPGLQPG
fz/Dros	SSA-----STAATPTRSVA
fz2/Dros/	TEAGSGGSSG---GSGG---SGSGSGGGKRQGGSGSGSGAGGSSGSTTKPCR-GR amino terminal domain continued

TM1	
fz3/mouse	YSFLHVRDCSPPCPN-----MYFRREELSFARYFIGLISIICLSATLFTFLTFLIDVTR
fz4/mouse	--LNCVLKCGYDAG-----LYSRSAKEFTDIWMAVWASLCFISTTFTVLTFLIDSSR
fz8/mouse	-KTGQIANCALPCHN-----PFFSQDERAFTVFWIGLWSVLCFVSTFATVSTFLIDMER
fz5/human	-RTGQVPNCAPCYQ-----PSFSADERTFATFWIGLWSVLCFISTSTTVATFLIDMDT
fzd9/human	--RSCAPRCGPGV-----FWSRRDKDFALVWMAWWSALCFSTAFFTFLTFLLEPHR
fz1/rat	LGEK---DCGAPCEPTKVYGLMYFGPEELRFSRTWIGIWSVLCCASTLFTVLTYLVDMRR
fz2/rat	LGER---DCAAPCEPARPDGSMFFSHHTRFARLWLTWSVLCCASTFFTFTTSLVAMQR
fz/Dros	VGGKDLHDCGAPCH-----AMFFPERERTVLRYWVGSWAAVCVASCLFTVLTFLIDSSR
fz2/Dros/	QRIAGVPNCIPCKG-----PFFSNDKDFAGLWIALWSGLFCSTLMTLTTFIIDTER

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TM2 → extracellular domain loop 1	
fz3/mouse	FRYPERPIIFYAVCYMMVSLIFFIGFLLE-DRVACNASSP-----
fz4/mouse	FSYPERPIIFLSMCYNIYSIAYIVRLTVGRERISCDF-----
fz8/mouse	FKYPERPIIFLSACYLFVSVGVLVRLVAGHEKVACSGGAPGAGGRGGAGGAAAGAGAAG
fz5/human	FRYPERPIIFLSACYLCVSLGFLVRLVVGHASVACS-----
fzd9/human	FQYPERPIIFLSMCNVYSLAFLIRAVAGAQSVACD-----
fz1/rat	FSYPERPIIFLSGCYTAVAVAYIAGFLLE-DRVVCNDKFAE-----
fz2/rat	FRYPERPIIFLSGCYTMSVAVYIAGFVLQ-ERVVCNERFSE-----
fz/Dros	FRYPERAIVFLAVCYLVVGCAVAGLGAG-DSVSCREPFPVVK--LG-----
fz2/Dros/	FKYPERPIVFLSACYFMVAVGYLSRNFLQNEEIACDG-----

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FIG. 2B

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TM3

fz3/mouse	-----AQYCASTVTQGSHNK-ACTMLFMVLYFFTMAGSVWWVILITTWFLA
fz4/mouse	-----EEAAEPVLIQEGLKNTGCAIIFLMYYFGMASSIWWVILTLTWFLA
fz8/mouse	RGASSPGARGEYEELGAVEQHVRYETTPALCTVVFLLVYFFGMASSIWWVILSLTWFLA
fz5/human	R-----EHNHIHYETTPALCTIVFLVYFFGMASSIWWVILSLTWFLA
fzd9/human	-----QEAGALYVIQEGLENTGCTLVFLLYFGMASSLWWVILTLTWFLA
fz1/rat	-----DGARTVAQGKKE-GCTILFMMLYFFSMASSIWWVILSLTWFLA
fz2/rat	-----DGYRTVGQGKKE-GCTILFMMLYFFSMASSIWWVILSLTWFLA
fz/Dros	-----RLQMMSTITQGHRQTTCTVLFMALYFCCMAAFAAWSCLAFAWFLA
fz2/Dros/	-----LLLRESSTGPHSCTLVFLLTYFFGMASSIWWVILTFWTWFLA

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TM4 → extracellular domain loop 2 ←

fz3/mouse	AVPKWGSEAIKKALLFHASAWGIPGTLTIILLAMNKIEGDNIISGVCFVGLYVDALRYF
fz4/mouse	AGLKWGHEAIEMHSSYFHIAAWAI PAVKTIVILIMRLVDADELGLCYVGNQNLDALTGF
fz8/mouse	AGMKWGNEAIAGYSQYFHLAAWLVPVKSIAVLALSSVDGDPVAGICYVGNQSLDNLRGF
fz5/human	AAMKWGNEAIAGYQYFHLAAWLIPVKSIATLALSSVDGDPVAGICYVGNQNLNSLRRF
fzd9/human	AGKKWGHEAIEAHGSYFHMAAWGLPAKLTIVILTRKVAGDELGLCYVASTDAAALTGF
fz1/rat	AGMKWGHEAIEANSQYFHLAAWAVPAIKTITILALQVQDGVLSGVCFVGLNNVDALRGF
fz2/rat	AGMKWGHAIEANSQYFHLAAWAVPAVKTITILAMQIDGDLISGVCFVGLNRDPLRGF
fz/Dros	AGLKWGHEAIENKSHLFHLVAWAVPAQQTISVLALAKVEGDILSGVCFVGQLDTHSLGAF
fz2/Dros/	AGLKWGNEAITKHSQYFHLAAWLIPTVQSVAVLLSAVDGDPILGICYVGNLNPDHLKTF

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TM5

fz3/mouse	VLAPLCLYVVGVSLLLAGIISLNVRVIEIPLEKE----NQDKLVKFMIRIGVFSILYL
fz4/mouse	VVAPLFTYLVIGTLFIAAGLVALFKIRSNLQK-DG----TKTDKLERLMVKIGVFSVLYT
fz8/mouse	VLAPLVIYLFIGTMFLLAGFVSLFRIRSVIKQQGGP---TKTHKLEKLMIRLGLFTVLYT
fz5/human	VLGPIVLYLLVGTFLLAGFVSLFRIRSVIKQ-GG----TKTDKLEKLMIRIGIFTLLYT
fzd9/human	VLVPLSGYLVLGSSFLLTGFVALFHIRKIMKT-GG----TNTEKLEKLMVKIGVFSILYT
fz1/rat	VLAPLFVYLFIGTSFLLAGFVSLFRIRTIMKH-DG----TKTEKLEKLMVRIGVFSVLYT
fz2/rat	VLAPLFVYLFIGTSFLLAGFVSLFRIRTIMKH-DG----TKTEPLERLMVRIGVFSVLYT
fz/Dros	LILPLCIYLSIGALFLLAGFISLFRIRTVMKT-DG----KRTDKLERLMLRIGFFSGLFI
fz2/Dros/	VLAPLFVYLVIGTTFLMAGFVSLFRIRSVIKQOQGGVGAGVKADKLEKLMIRIGIFSVLYT

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FIG. 2C

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TM6	extracellular domain loop 3	↔
fz3/mouse	VPLLVIGCYFYEQAYRGIWETTWIQCERCREYHIPCPCYQVTQMS-----	RPDLILFLM
fz4/mouse	VPATCVIACYFYEISNWALFRYSADDS-----	NMAVEML
fz8/mouse	VPAAVVAACLFYEQHNRPRWEATHNCPLRDQLQPDQARR-----	PDYAVFML
fz5/human	VPASIVVACLYEQHYRESWEAALTACPGHDTGQPRAK-----	PEYWVML
fzd9/human	VPATCVIVCYVYERLNMDFWRLRATEQPCAAAAGPGGRRDCSLP---	GGSVPTVAVFML
fz1/rat	VPATIVIACYFYEQAFRDQWERSWVAQSCSKSYAIPCPHLQGGGGVPPHPMPSPDFTVFMI	
fz2/rat	VPATIVIACYFYEQAFREHWERSWVSQHCKSLAIPCPAHYT-----	PRTSPDFTVYMI
fz/Dros	LPAVGLLGCLFYEYYNDFEWMIQWHRDICKPFSIPCPAARAPGS---	PEARPIFQIFMV
fz2/Dros/	VPATIVIGCYLYEAYFEDWIKALACPCAQVK--GPGKK-----	PLYSVLM
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TM7		
fz3/mouse	KYLMALIVGIPSIFWVGSKKTCFEWASFFHGRRKKEIVNESRQLQEPDFAQSLLRDPNT	
fz4/mouse	KIFMSLLVGITSGMWIWSAKTLHTWQKCS-----	NRLVNSGKV-----REKRG
fz8/mouse	KYFMCLVVGITSGVWWSGKTLESWRALC-----	TRCCWASKGAAVGAGAGGSG
fz5/human	KYFMCLVVGITSGVWIWSGKTVESWRRT-----	SRCCRPR-----RGHK-
fzd9/human	KIFMSLVVGITSGVWWSSKTFQTWQSLC-----	YRKIAAGRARA---KACRA
fz1/rat	KYLMTLIVGITSFGWIWSGKTLNSWRKFY-----	TRLTNSK-----QGETT
fz2/rat	KYLMTLIVGITSFGWIWSGKTLHSWRKFY-----	TRLTNSR-----HGETT
fz/Dros	KYLCMSLVLGVTSVWLYSSKTMVSWRNFV-----	ERLQGKEPRT-----RAQAY
fz2/Dros/	KYFMALAVGITSFGWIWSGKTLESWRRFW-----	RRLLGAPDRTGANQALIKQR
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FIG. 2D

Sequence alignment of a portion of the aminoterminal extracellular region of human Frizzled receptors

HFZ1	VGQNTSDKGT---PSLLPEFWTSNPQHGGGGHRG-----	GFPGGAG---ASERGKFSCPR
HFZ2	VGQNHSEDGA---PALLTAPPGLQPGAGGTPG-----	GPGGGGAPPYATLEHPFHC
HFZ3	LVDLNLAG---EPTEGAPV-----	AVQRDYG-----FWC
HFZ4	CMEGPGD---EE-----	VPLPHKTP-----QP
HFZ5	CMDYNRSEATTAPPRPFPAKPTLPG-----PPGA-----	PASGG-----ECPAGGPVF-----CKC
HFZ6	TFDPHTEF---LGPQKKTE-----	QVQRDYG-----FWC
HFZ7	VGQNTSDGSGGPCCGPTAYPTAPYLPDLPFTALPG-----	ASDGRGRPAF-----PFSC
HFZ8	CMDYNRTDLTTAAPSPPRRLPPPPP-----GEQPPSGSGHGRPPGARPHRGGRGGGGDAAAPPARGGGGGKARPPGGAAP---	CEPGQC
HFZ9	CMEAPENA-TAGPAEPHKGLMLPV-----	APRPARPPG-----DLGP
HFZ10	NYLCMEAPNN---GSDEPTRGSGLFPP-----	LFRPQRPHSAQ---EHP

FIG. 3

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Effect of FZD on SNU1076 cells

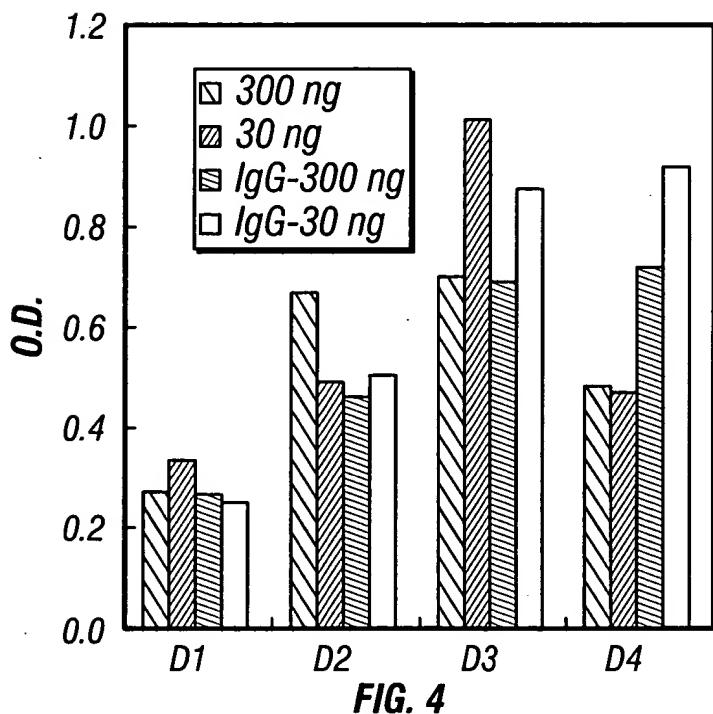


FIG. 4

Effect of antibodies SNU 1076 Cells

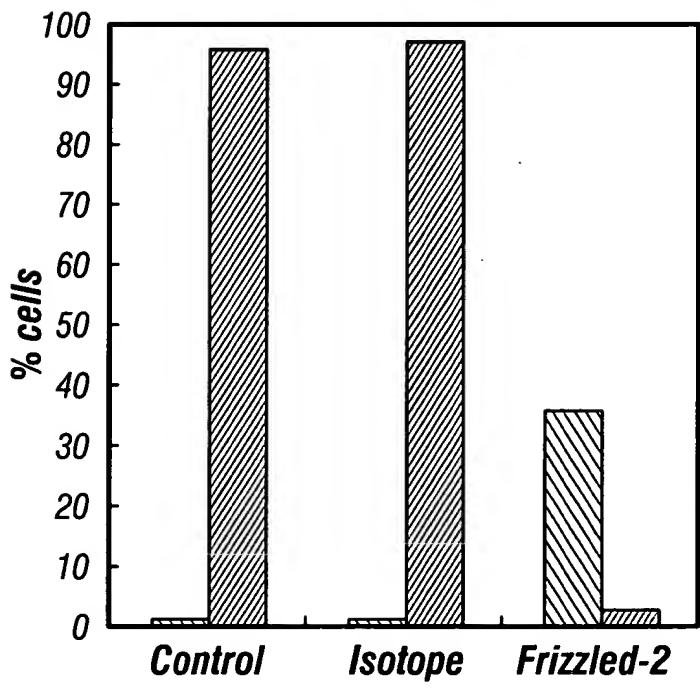


FIG. 5

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Graphical Representation of an Olfactory Protein showing Aminoterminal and three Extracellular Domain Loops (from PCT WO 92/17585)

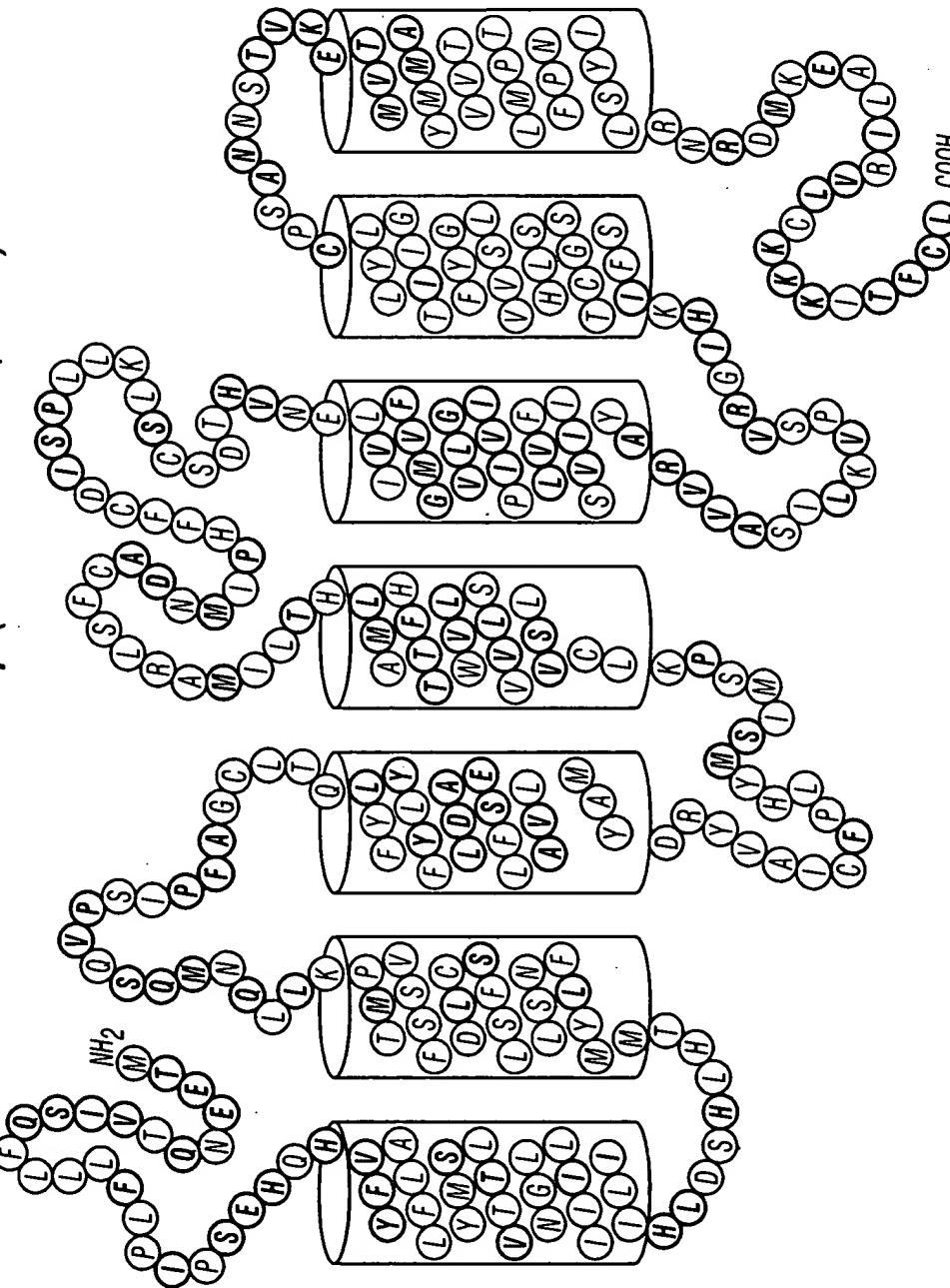


FIG. 7

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Effect of antibodies SNU 1076 Cells

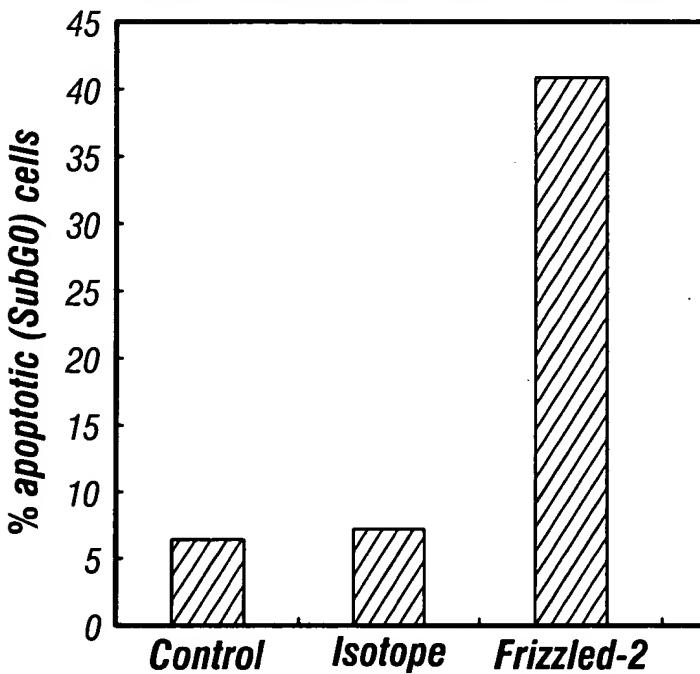


FIG. 6

↑ amino terminal domain

HFZ1	MAEEEAPKSRAAGGGASWELCAGALSARLAEEGSGDAGGRRPPVDPRLARQLLLLLW
MFZ1	MAEEAAPSSESRAAGR-LSLELCAEALPGRREEVGHEDTASHRRPRADPRRWASGLLLLLW
HFZ2	-----MRPRSAALPRLLLPLL
HFZ3	-----MAMTWIVFSLWPLTV
MFZ3	-----MAVSWIVFDLWLTV
HFZ4	-----MAWRGAGPSVPVGAPGGVGLSLGLLLQ
MFZ4	-----MAWPGTGPSRGAPGGVGLRLGLLQ
HFZ5	-----MARPDPSAPPSSL-L--LLL
MFZ5	-----MEMFTFLLCI
HFZ6	-----MERSPFLLACI
MFZ6	-----MRDPGAAAPLSSLGLCALVLA
HFZ7	-----MRGPGTAASHSPLGLCALVLA
MFZ7	-----MEWGYLLEVTSLLAALAL
HFZ8	-----MEWGYLLEVTSLLAALAV
MFZ8	-----MAVAPL-RGALLWQLLA
HFZ9	-----MAVPPLLRGALLWQLLA
MFZ9	-----MQRPGPRLWIVLQ
HFZ10	-----

FIG. 8A

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HFZ1	LLEAPLLLGVRAQAAQGPQGPQGPQOPPPQQQSGQQYNGERGISVPDHGQCPIS
MFZ1	LLEAPLLLGVRAQAAQGVSG---PGQQAPPPPQGPQSGQQYNGERGISIPDHGQCPIS
HFZ2	LLPA-----A-----GPAQFHGEKGISIPDHGFCQPI
HFZ3	FMGHI-----GGHSLFS-----CEPIT
MFZ3	FLGQI-----GGHSLFS-----CEPIT
HFZ4	LLLLLG-----PARGFGDEEE-----RRCDPIR
MFZ4	FLLLR-----PTLGFGEDEEE-----RRCDPIR
HFZ5	LAQLVG-----RAAAASKAPV-----CQEIT
HFZ6	FLPLL-----RGHSLFT-----CEPIT
MFZ6	LLPLV-----RGHSLFT-----CEPIT
HFZ7	LLGAL-----SAGAGAQPYHGEKGISVPDHGFCQPI
MFZ7	LLGAL-----PTDTRAQPYHGEKGISVPDHGFCQPI
HFZ8	LQRSSG-----AAAASAKELA-----CQEIT
MFZ8	LQRSSG-----AAAASAKELA-----CQEIT
HFZ9	AGGAAL-----EIGRFDPERGR-----GAAPCQAVE
MFZ9	TGGAAL-----EIGRFDPERGR-----GPAPCQAME
HFZ10	VMGSCA-----AISSMDMERP-----GDGKCQPI

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HFZ1	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVCT-V
MFZ1	IPLCTDMAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVCT-V
HFZ2	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
HFZ3	LRMCQDLPYNTTFMPNLLNHYDQTAALAMEPFHPMVNLDCSRDFRFLCALYAPICM-E
MFZ3	LRMCQDLPYNTTFMPNLLNHYDQTAALAMEPFHPMVNLDCSRDFRFLCALYAPICM-E
HFZ4	ISMCQNLGYNVTKMPNLVGHELQTDALQLTFTPLIQQGSSQLQFFLCSVYVPMCTEK
MFZ4	IAMCQNLGYNVTKMPNLVGHELQTDALQLTFTPLIQQGSSQLQFFLCSVYVPMCTEK
HFZ5	VPMCRGIGYLNTHMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPDLRFLLCTMYTPICLD
HFZ6	VPRCMKMAYNMTFFPNLMGHYDQSIAAVEMEHFLPLANLECSPIETFLCAFVPTCI-E
MFZ6	VPRCMKMTYNMTFFPNLMGHYDQGIAAAVEMGHFLHLANLECSPIEMFLCQAFIPTCT-E
HFZ7	IPLCTDIAYNQTILPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
MFZ7	IPLCTDIAYNQTILPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
HFZ8	VPLCKGIGYNYTYMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPDLKFLLCSMYTPICLED
MFZ8	VPLCKGIGYNYTYMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPDLKFLLCSMYTPICLED
HFZ9	IPMCRGIGYLNTRMPNLLGHTSQGEAAELAEFAPLVQYQGCHSHLRFLCSLYAPMCTDQ
MFZ9	IPMCRGIGYLNTRMPNLLGHTSQGEAAQLAEFSPLVQYQGCHSHLRFLCSLYAPMCTDQ
HFZ10	IPMCKDYGYNMTRMPNLMGHENQREAAIQLHEFAPLVEYQGCHSHLRFLCSLYAPMCTEQ

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FIG. 8B

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HFZ1	LEQALPPCRSLCERARQCEALMNKFGFQWPDTLKCEKFPVHG--AGELCVGQNTSDKGT
MFZ1	LEQALPPCRSLCERARQCEALMNKFGFQWPDTLKCEKFPVHG--AGELCVGQNTSDKGT
HFZ2	LEQAIPPCRSICERARQCEALMNKFGFQWPRLCEHFPRHG--AEQICVGQNHSEDGA
HFZ3	YGRVTLPCRRLCQRAYSECSKLMEMFGVPWPEDMECSRFPDCD-EPYPRLVLDNLAG---
MFZ3	YGRVTLPCRRLCQRAYSECSKLMEMFGVPWPEDMECSRFPDCD-EPYPRLVLDNLVG---
HFZ4	INIPIGPCGGMCLSVRRCEPVLKEFGFAWPESLNCSKFPPQN-DHNHMCMEGPGD---
MFZ4	INIPIGPCGGMCLSVRRCEPVLREFGFAWPDTLNCSKFPPQN-DHNHMCMEGPGD---
HFZ5	YHKPLPPCRSVCERAKAGCPLMRQYGFAWPERMCDRLPVLGRDAEVLCMDNRSEATT
HFZ6	QIHVVPPCRKLCEVKYSDCKKLIDTFIGIRWPEELECDRLQYCD-ETPVTFDPHTEF---
MFZ6	QIHVVLPCKLCEKIVSDCKLMDTFIGIRWPEELECNRLPHCD-DTVPTSHPTEL---
HFZ7	LDQAIAPPCKLCEKAGCPLMRQYGFQWPRLRCENFPVHG--AGEICVGQNTSDGSG
MFZ7	LDQAIAPPCKLCEKAGCPLMRQYGFQWPRLRCENFPVHG--AGEICVGQNTSDGSG
HFZ8	YKKPLPPCRSVCERAKAGCPLMRQYGFAWPDRMRCDRLEQG-NPDTLCMDYNRTDLTT
MFZ8	YKKPLPPCRSVCERAKAGCPLMRQYGFAWPDRMRCDRLEQG-NPDTLCMDYNRTDLTT
HFZ9	VSTPIPACRPMCEQARLRCAPIMEQFNFGWPDSLDCARLPTRN-DPHALCMEAPENA-TA
MFZ9	VSTPIPACRPMCEQARLRCAPIMEQFNFGWPDSLDCARLPTRN-DPHALCMEAPENA-TA
HFZ10	VSTPIPACRVMCEQARLKCSPIMEQFNFKWPDSLDCRKLPNKN-DPNYLCMEAPNN---

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HFZ1	PT---PSLLPEFWTSNPQHGGGGHRG-----
MFZ1	PT---PSLLPEFWTSNGQHGGGGYRG-----
HFZ2	-----PALLTAPPGLQPGAGGTPG-----
HFZ3	-----EPTEGAPV-----A
MFZ3	-----DPTEGAPV-----A
HFZ4	-----EE-----V
MFZ4	-----EE-----V
HFZ5	APPRPFPAKPTLPG-----PPGA-----PASGG-----
HFZ6	---LGPQKKTE-----Q
MFZ6	---SGPQKKSD-----Q
HFZ7	GPGGGPTAYPTAPYLPDLPFTALPPG-----
MFZ7	GAGGSPTAYPTAPYLPDPPFTAMSP-----
HFZ8	AAPSPPRLLPPP----GEQPPSGSGHGRPPGARPPHRRGGGGGGDAAAPPARGGGGGK
MFZ8	AAPSPPRLLPPPPPGEQPPSGSGHSRPPGARPPHRRGGSSRGSGDAAAAPPSSRGK-----K
HFZ9	GPAEPHKGLGMLPV-----A
MFZ9	GPTEPHKGLGMLPV-----A
HFZ10	GSDEPTRGSGLFPP-----L

FIG. 8C

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HFZ1	GFPGGAG---ASERGKFSCPRAKVP SYL NYHFLGEKDCGAPCEPTK VYGL MYFGPEEL
MFZ1	GYPGGAG---TVERGKFSCPRA LRVPS YL NYHFLGEKDCGAPCEPTK VYGL MYFGPEEL
HFZ2	GPGGGGAPP RYATLEHPFHCP RLKVPS YL SYKFLGERD CAA PCEPARPDGSMFFSQEET
HFZ3	VQR DYG-----FWCP RELKIDPDLGYSFLHVRDCSPPCP---NMYFR--REEL
MFZ3	VQR DYG-----FWCP RELKIDPDLGYSFLHVRDCSPPCP---NMYFR--REEL
HFZ4	PLPHKTPI-----QPGE ECHS VGTNSDQYIWVKRS LNCVLKCGYDAGLY-SRSAK
MFZ4	PLPHKTPI-----QPGE ECHS VGSNSDQYIWVKRS LNCVLKCGYDAGLY-SRSAK
HFZ5	ECPAGGP FV-----CKCREPFV PILKES HPLYNKV RTGQV PNC AVPCYOPS F SADER
HFZ6	VQR DIG-----FWCP RLKTS GGQGYKFLGIDQ CAPP C P---NMYFK--SDEL
MFZ6	VPR DIG-----FWCP KHLRTSGDQGYRFLGIEQCAPP C P---NMYFK--SDEL
HFZ7	ASDGRGRPAF-----PFSCPRQLK VPPYLGYRFLGERDCGAPCEPGRANGL MYFKEER
MFZ7	-SDGRGRLSF-----PFSCPRQLK VPPYLGYRFLGERDCGAPCEPGRANGL MYFKEER
HFZ8	ARPPGGGAAP---CEPGCQC RAPM VS SSERHPLYN RVKTGQIAN CALPCHNPFFSQDER
MFZ8	ARPPGGGAAP---CEPGCQC RAPM VS SSERHPLYN RVKTGQIAN CALPCHNPFFSQDER
HFZ9	PRPARPPG-----DLGP GAGGSGT CENPEKFQYVEKSRSCAPRCGP GVEV FW SRRDK
MFZ9	PRPARPPG-----DSAPGP GSGG TCDNPEKFQYVEKSRSCAPRCGP GVEV FW SRRDK
HFZ10	FRPQRPHSAQ---EHPLKDGGPGRGGCDNPGKFHHVEKSASCAPLCTPGVDVYWSREDK

HFZ1	RFSRTWIGIWSVLCCASTLFTVL TLYLVD MRRFSYPERPIIFLSGCYTA VAVAYIAGFLLE
MFZ1	RFSRTWIGIWSVLCCASTLFTVL TLYLVD MPRFSYPERPIISLSGCYTA VAVAYIAGFLLE
HFZ2	RFARLWILTWSVLCCASTFFT VTTLYLVD MQRFRYPERPIIFLSGCYTMVSVAYIAGFLQ
HFZ3	SFARYFIGLISIICLSATLFTFLFLIDVTRFRYPERPIIFYAVCYMMVSLIFFIGFLLE
MFZ3	SFARYFIGLISIICLSATLFTFLFLIDVTRFRYPERPIIFYAVCYMMVSLIFFIGFLLE
HFZ4	EFTDIWMAWASLCFIST AFTVLTFLIDSSRFSYPERPIIFLSMCYNIY SIAYIVRLTVG
MFZ4	EFTDIWMAWASLCFIST TTVLTFLIDSSRFSYPERPIIFLSMCYNIY SIAYIVRLTVG
HFZ5	TFATFWIGLWSVLCFISTSTT VATFLIDMDTFRYPERPIIFLSAC YLCVSLGFLVRLVVG
HFZ6	EFAKSFIGTVSIFCLCATLFTFLFLIDVRRFRYPERPII YY SVCY SIVSLM YFIGFLLG
MFZ6	DFAKSFIGIVSIFCLCATLFTFLFLIDVRRFRYPERPII YY SVCY SIVSLM YFIGFLLG
HFZ7	RFARLWVGWWSVLCCASTLFTVL TLYLFD MRRFSYPERPIIFLSGCYFMVAVAHVAGFLLE
MFZ7	RFARLWVGWWSVLCCASTLFTVL TLYLFD MRRFSYPERPIIFLSGCYFMVAVAHVAGFLLE
HFZ8	AFTVFWIGLWSVLCFVSTFATVSTFLIDMERFKYPERPIIFLSAC YLFVSVG YLVR L VAG
MFZ8	AFTVFWIGLWSVLCFVSTFATVSTFLIDMERFKYPERPIIFLSAC YLFVSVG YLVR L VAG
HFZ9	DFALVWMAWWSALCFSTAFTVLTFLLEPHRFQYPERPIIFLSMCYNVYSLAFLIRAVAG
MFZ9	DFALVWMAWWSALCFSTAFTVFTFLLEPHRFQYPERPIIFLSMCYNVYSLAFLIRAVAG
HFZ10	RFAVWVLAIAW VLCFSSAFTVLTFLIDPARFRYPERPIIFLSMCYCVSVG YLIRLFAG

*: :: : : . :: * . *: *: * * ***** : ** :: ..

FIG. 8D

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→ extracellular domain loop 1

HFZ1	DRVVCNDK	FAEDGARTVAQGTTKK
MFZ1	DRVVCNDK	FAEDGARTVAQGTTNK
HFZ2	ERVVCNER	FSEDGYRTVVQGTTKK
HFZ3	DRVACNAS	I PAQYKASTVTQGSHN
MFZ3	DRVACNAS	S PAQYKASTVTQGSHN
HFZ4	RERISCDF	EEAAEPVLIQEGLKN
MFZ4	RERISCDF	EEAAEPVLIQEGLKN
HFZ5	HASVACS	RE HNHIHYETTGP
HFZ6	DSTACNKA	D EKLELGDTVVLGSN
MFZ6	NSTACNKA	D EKLELGDTVVLGSKN
HFZ7	DRAVCVER	FSDDGYRTVAQGTTKK
MFZ7	DRAVCVER	FSDDGYRTVAQGTTKK
HFZ8	HEKVACSGGAPGAGGAGGAGGAAA-GAGAAGAGAGGPGGRGEYEELGAVEQHVRYETTGP	
MFZ8	HEKVACSGGAPGAGGRGGAGGAAAAGAGAAGRGASSPGARGEYEELGAVEQHVRYETTGP	
HFZ9	AQSVACD	QEAGALYVIOEGLEN
MFZ9	AQSVACD	QEAGALYVIQEGLEN
HFZ10	AESIACD	RDSGQLYVIQEGLES

1

HFZ1	EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAIKT
MFZ1	EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAIKT
HFZ2	EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
HFZ3	KACTMLFMILYFFT MAGSVWWVILTITWFLA AVPKWGSEAIEKKALLFHASAWGIPGTLT
MFZ3	KACTMLFMVLYFFT MAGSVWWVILTITWFLA AVPKWGSEAIEKKALLFHASAWGIPGTLT
HFZ4	TGCAIIFLLMYFFGMASSIWWVILTLTWFLAAGLKWGHEAIEMHSSYFHIAAWAI PAVKT
MFZ4	TGCAIIFLLMYFFGMASSIWWVILTLTWFLAAGLKWGHEAIEMHSSYFHIAAWAI PAVKT
HFZ5	ALCTIVFLLVYFFGMASSIWWVILSLTWFLAAAMKGNEIAGYQYFHLAAWLIPSVKS
HFZ6	KACTVLFMLLYFFT MAGTVWWVILTITWFLAAGRKSCEAIEQKAVWFHAVA WGTGFLT
MFZ6	KACSVVFMFLYFFT MAGTVWWVILTITWFLAAGRKSCEAIEQKAVWFHAVA WGA PGFLT
HFZ7	EGCTILFVLYFFGMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
MFZ7	EGCTILFVLYFFGMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
HFZ8	ALCTVVFLLVYFFGMASSIWWVILSLTWFLAAGMKWGNEIAGYSQYFHLAAWL VPSVKS
MFZ8	ALCTVVFLLVYFFGMASSIWWVILSLTWFLAAGMKWGNEIAGYSOYFHLAAWL VPSVKS
HFZ9	TGCTLVFLYYFGMASSLWWVLTLTWFLAAGKKWGHEAIEAHGSYFHM AAWGLPALKT
MFZ9	TGCTLVFLYYFGMASSLWWVLTLTWFLAAGKKWGHEAIEAHGSYFHM AAWGLPALKT
HFZ10	TGCTLVFLVLYFGMASSLWWVLTLTWFLAAGKKWGHEAIEANSSYFHLAAWAI PAVKT

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→ extracellular domain loop 2 ←

HFZ1	ITILALGQVDGVLSGVCVGLNNDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
MFZ1	ITILALGQVDGVLSGVCFLGLNNDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
HFZ2	ITILAMQIDGDLLSGVCFVGLNSLDPLRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
HFZ3	IILLAMNKIEGDNISGVCFVGLYDVDALRYFVLAPLCLYVVVGVSLLAGIISLNVRVIE
MFZ3	IILLAMNKIEGDNISGVCFVGLYDVDALRYFVLAPLCLYVVVGVSLLAGIISLNVRVIE
HFZ4	IVILIMRLVDAELETGLCYVGNQNLDALTGFVAPLFTYLVIGTLFIAAGLVALFKIRSN
MFZ4	IVILIMRLVDAELETGLCYVGNQNLDALTGFVAPLFTYLVIGTLFIAAGLVALFKIRSN
HFZ5	ITALALSSVGDGPVAGICYVGNQNLSLRRFVLGPLVLYLLVGTFLLAGFVSLFRIRSV
HFZ6	VMLLAMNKVEGDNISGVCFVGLYDLDASRYFVLLPLCLCVFVGLSLLAGIISLNHVRQV
MFZ6	VMLLAMNKVEGDNISGVCFVGLYDLDASRYFVLLPLCLCVFVGLSLLAGIISLNHVRQV
HFZ7	ITILAMQVDGDLLSGVCYVGLSSVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
MFZ7	ITILAMQVDGDLLSGVCYVGLSSVDALRGFVLAPLFVVLFIGTSFLLAGFVSLFRIRTI
HFZ8	IAVLALSSVGDGPVAGICYVGNQSLDNLRGFVLAPLVIYLFIGTMFLLAGFVSLFRIRSV
MFZ8	IAVLALSSVGDGPVAGICYVGNQSLDNLRGFVLAPLVIYLFIGTMFLLAGFVSLFRIRSV
HFZ9	IVILTLRKVAGDELTGLCYVASTDAAALTGFVLVPLSGYLVLGSSFLTGVALFHIRKI
MFZ9	IVVLTLRKVAGDELTGLCYVASMDPAALTGFVLVPLSCYLVLGTSFLTGVALFHIRKI
HFZ10	ILILVMRRVAGDELTGVCYVGSMVDVNALTGFVLIPACYLFIGTSFILSGFVALFHIRRV

► extracellular domain loop 3

FIG. 8F

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HFZ1	AIPCPHLQAGGGAPPHPMPSPDFTVFMIKYLMTLIVGITSGFWIWSGKTLNSWRKFYTRL
MFZ1	AIPCPHLQGGGVPPHPMPSPDFTVFMIKYLMT-----LNSWRKFYTRL
HFZ2	AIPCP----AHYTPR--MSPDFTVYMIKYLMTLIVGITSGFWIWSGKTLHSWRKFYTRL
HFZ3	HIPCP-----YQVTQMSRPDLILFLMKYLMALIVGIPSVFWVGSKKTCFEWASFFHGR
MFZ3	HIPCP-----YQVTQMSRPDLILFLMKYLMALIVGIPSI FWVGSKKTCFEWASFFHGR
HFZ4	-----EMLKIFMSLLVGITSGMWIWSAKTLHTWQ-KCSNR
MFZ4	-----EMLKIFMSLLVGITSGMWIWSAKTLHTWQ-KCSNR
HFZ5	TGQPR---AK-----PEYWVILMKYFMCLVVGIGITSGFWIWSGKTVESWRRTSRC
HFZ6	HIPCP-----YQAKAKARPELALFMIKYLMTLIVGIGAVFWVGSKKTCTEWAGFFKRN
MFZ6	RIPCP-----YQANPKARPELALFMIKYLMTLIVGIGAVFWVGSKKTCTEWAGFFKRN
HFZ7	AVPCP---PGHFPPM---SPDFTVFMIKYLMTMIVGIGITGFWIWSGKTLQSWRRFYHRL
MFZ7	AVPCP---PRHFSPM---SPDFTVFMIKYLMTMIVGIGITGFWIWSGKTLQSWRRFYHRL
HFZ8	QPDQA---RR-----PDYAVFMLKYFMCLVVGIGITSGVWVWSGKTLESWRSLCTRC
MFZ8	QPDQA---RR-----PDYAVFMLKYFMCLVVGIGITSGVWVWSGKTLESWRALCTRC
HFZ9	AGPGG---RRDCSLPGGSVPTVAVFMLKIFMSLVVGIGITSGVWVWSKTFQTWQSLCYRK
MFZ9	TVPGG---RRDCSLPGGSVPTVAVFMLKIFMSLVVGIGITSGVWVWSKTFQTWQSLCYRK
HFZ10	NNQTK---TLDC-LMAASIPAVEIFMVKIFMLLVVGIGITSGMWIWTSTKTLQSWQQVCRR

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HFZ1	TN--SKQGETTV-----
MFZ1	TN--SKQGETTV-----
HFZ2	TN--SRHGETTV-----
HFZ3	RKKEIVNESRQLQEP-----DFAQSLLRDPNTPIIRKSRGSTQGTSTHAS
MFZ3	RKKEIVNESRQLQEP-----DFAQSLLRDPNTPIIRKSRGSTQGTSTHAS
HFZ4	LVNSGKVKREKRGNGW-----VKPGKGSE-----
MFZ4	LVNSGKVKREKRGNGW-----VKPGKGNE-----
HFZ5	CC-RPRRGHKSGGA-----MA--AG-D-----
HFZ6	RKRDPISESRRVLQESCEFFLKHNSKVKHKKKHYKPSSHLKVISKSMGTSTGATANHGT
MFZ6	RKRDPISESRRVLQESCEFFLKHNSKVKHKKKHGAPGPHRLKVISKSMGTSTGATTNHGT
HFZ7	SH--SSKGETAV-----
MFZ7	SH--SSKGETAV-----
HFZ8	CW-ASKGAAVGGGAGA-----TAAGGGGGPGGGGGGP
MFZ8	CW-ASKGAAVGAGAGG-----SGPGGSGP-----GP
HFZ9	IA--AGRARAKACRAP-----GSYGRGTHC-----
MFZ9	MA--AGRARAKACRTP-----GGYGRGTHC-----
HFZ10	LKKKSRRKPASVITSG-----GIYKKAQH-----

FIG. 8G

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HFZ1
MFZ1
HFZ2
HFZ3 STQLAMVDDQRSKAGSIHSKVSSYH GSLHRSRDGRYTPCSYRG--MEERLPHGSMS-RLT
MFZ3 STQLAMVDDQRSKAGSVHSKVSSYH GSLHRSRDGRYTPCSYRG--MEERLPHGSMS-RLT
HFZ4 -----TVV-----
MFZ4 -----TVV-----
HFZ5 -----YPEASAALTGRTGPPGPAATYHKQVSLSHV-----
HFZ6 SAVAITS HDYLQETLITEIQTSPETSMREVKADGASTPRLREQDCGE PASPAASIS-RLS
MFZ6 SAMAIADHDYLQETSTEVHTSPEASVKEGRADRANTPSAKDRDCGESAGPSSKLSGNRN
HFZ7
MFZ7
HFZ8 GGGGGPGGGGGSLYSDVSTGLTWRSGTAS-SVSYPKQMPPLSQV-----
MFZ8 GGGGGHGGGGSLYSDVSTGLTWRSGTAS-SVSYPKQMPPLSQV-----
HFZ9 -----H--YKAPTVVLHMTKTDPSLENPTHL-----
MFZ9 -----H--YKAPTVVLHMTKTDPSLENPTHL-----
HFZ10 -----PQKT-HHGKYEIPAQSPTCV-----

HFZ1
MFZ1
HFZ2
HFZ3 DHSRHSSSHRLNEQSRHSSIRDLSNNPMTHITHGTSMNRVIEEDGTSA-----
MFZ3 DHSRHSSSHRLNEQSRHSSIRDLSNNPMTHITHGTSMNRVIEEDGTSA-----
HFZ4
MFZ4
HFZ5
HFZ6 GEQVDGKG--QAGSVSESARSEG RISPKSDITDTGLAQSNNLQVPSSSEPSSLKGSTSLL
MFZ6 GRESRAGGLKERSNGSEGAPSEGRVSPKSSVPETGLIDCSTSQAASSPEPTSLKGSTS LP
HFZ7
MFZ7
HFZ8
MFZ8
HFZ9
MFZ9
HFZ10

FIG. 8H

Title: IMMUNOLOGIC COMPOSITIONS AND METHODS FOR STUDYING
AND TREATING CANCERS EXPRESSING FRIZZLED ANTIGENS
Inventor: Dennis A. Carson, et al.
Application No.: 09/847,102
Docket No.: 220002062900

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HFZ1	-----
MFZ1	-----
HFZ2	-----
HFZ3	-----
MFZ3	-----
HFZ4	-----
MFZ4	-----
HFZ5	-----
HFZ6	VHPVSGVRKEQGGGCHSDT
MFZ6	VHSASRARKEQGAGSHSDA
HFZ7	-----
MFZ7	-----
HFZ8	-----
MFZ8	-----
HFZ9	-----

FIG. 8I